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11. Document ID: US 6045996 A

L1: Entry 11 of 17

File: USPT

Apr 4, 2000

US-PAT-NO: 6045996

DOCUMENT-IDENTIFIER: US 6045996 A

TITLE: Hybridization assays on oligonucleotide arrays

DATE-ISSUED: April 4, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP	CODE	COUNTRY
Cronin; Maureen T.	Los Altos	CA			
Miyada; Charles Garrett	San Jose	CA			
Trulson; Mark	San Jose	CA			
Gingeras; Thomas R.	Encinitas	CA			
McGall; Glenn	Mountain View	CA			
Robinson; Claire	Palo Alto	CA			
Oval; Michelle	Coronado	CA			

US-CL-CURRENT: 435/6; 422/50, 422/68.1, 436/501

ABSTRACT:

This invention provides methods of performing $\underline{\text{nucleic}}$ acid hybridization assays on high-density substrate-bound oligonucleotide $\underline{\text{arrays}}$ involving including in the hybridization mixture an isostabilizing agent, a $\underline{\text{denaturing}}$ agent or a renaturation accelerant.

10 Claims, 2 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC

12. Document ID: US 6007987 A

L1: Entry 12 of 17

File: USPT

Dec 28, 1999

US-PAT-NO: 6007987

DOCUMENT-IDENTIFIER: US 6007987 A

TITLE: Positional sequencing by hybridization

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Cantor; Charles R. Boston MA
Przetakiewicz; Marek East Boston MA
Sano; Takeshi Boston MA
Smith; Cassandra L. Boston MA

US-CL-CURRENT: 435/6; 536/24.3

ABSTRACT:

This invention is directed to methods and reagents useful for sequencing nucleic acid targets utilizing sequencing by hybridization technology comprising probes, arrays of probes and methods whereby sequence information is obtained rapidly and efficiently in discrete packages. That information can be used for the detection, identification, purification and complete or partial sequencing of a particular target nucleic acid. When coupled with a ligation step, these methods can be performed under a single set of hybridization conditions. The invention also relates to the replication of probe arrays and methods for making and replicating arrays of probes which are useful for the large scale manufacture of diagnostic aids used to screen biological samples for specific target sequences. Arrays created using PCR technology may comprise probes with 5'-and/or 3'-overhangs.

7 Claims, 16 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 13

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13. Document ID: US 5795714 A

L1: Entry 13 of 17

File: USPT

Aug 18, 1998

US-PAT-NO: 5795714

DOCUMENT-IDENTIFIER: US 5795714 A

TITLE: Method for replicating an array of nucleic acid probes

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:

COUNTRY ZIP CODE CITY STATE NAME MA **Boston** Cantor; Charles R. Boston MA Przetakiewicz; Marek MA Boston Smith; Cassandra L. Boston MA Sano; Takeshi

US-CL-CURRENT: 435/6; 536/24.3, 536/24.33, 536/25.3

ABSTRACT:

The invention relates to the replication of probe arrays and methods for replicating arrays of probes which are useful for the large scale manufacture of diagnostic aids used to screen biological samples for specific target sequences. Arrays created using PCR technology may comprise probes with 5'- and/or 3'-overhangs.

29 Claims, 16 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 13



KWIC

14. Document ID: US 5624845 A

L1: Entry 14 of 17

File: USPT

Apr 29, 1997

US-PAT-NO: 5624845

DOCUMENT-IDENTIFIER: US 5624845 A

TITLE: Assembly and a method suitable for identifying a code

DATE-ISSUED: April 29, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Wickramasinghe; Hemantha K. Chappaqua NY Zenhausern; Frederic Mohegan Lake NY

US-CL-CURRENT: 435/287.2; 250/306, 250/311, 385/15, 385/31, 435/288.7

ABSTRACT:

An assembly suitable for identifying a code sequence of a biomolecule. The assembly includes means comprising a near-field probe for generating a super-resolution chemical analysis of the portion of a biomolecule; and means for correlating the super-resolution chemical analysis of the portion of the biomolecule with a broad spectral content of a referent biomolecule, for generating a code sequencing of the portion of the biomolecule.

9 Claims, 13 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 13



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15. Document ID: US 5609744 A

L1: Entry 15 of 17

File: USPT

Mar 11, 1997

US-PAT-NO: 5609744

DOCUMENT-IDENTIFIER: US 5609744 A

TITLE: Assembly suitable for identifying a code sequence of a biomolecule in a gel embodiment

DATE-ISSUED: March 11, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Zenharusern; Frederic Mohegan Lake NY Wickramasinghe; Hemantha K. Chappaqua NY

US-CL-CURRENT: 204/606; 204/616, 356/301, 356/318, 422/82.01, 422/82.08, 435/287.1,

435/287.2

ABSTRACT:

An assembly suitable for identifying a code sequence of at least a portion of a biomolecule in a gel embodiment. The assembly comprises first means for migrating and separating a portion of a biomolecule in a gel; second means comprising a near-field probe for generating a super-resolution chemical analysis of a portion of a biomolecule; and, third means for correlating the super-resolution chemical analysis of the portion of the biomolecule with a broad spectral content of a referent biomolecule, for generating a code sequencing of the portion of the biomolecule.

13 Claims, 13 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 13



KWIC

16. Document ID: US 5607568 A

L1: Entry 16 of 17

File: USPT

Mar 4, 1997

US-PAT-NO: 5607568

DOCUMENT-IDENTIFIER: US 5607568 A

TITLE: Assembly suitable for identifying a code sequence of a biomolecule in a free-solution embodiment

DATE-ISSUED: March 4, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Zenharusern; Frederic Mohegan Lake NY Wickramasinghe; Hemantha K. Chappaqua NY

US-CL-CURRENT: 204/600; 204/452, 204/456, 204/461, 204/603, 204/612

ABSTRACT:

An assembly suitable for identifying a code sequence of at least a portion of a biomolecule in a free-solution embodiment. The assembly comprises first means for migrating and separating a portion of a biomolecule in a free-solution; second means comprising a near-field probe for generating a super-resolution chemical analysis of a portion of a biomolecule; and, third means for correlating the super-resolution chemical analysis of the portion of the biomolecule with a broad spectral content of a referent biomolecule, for generating a code sequencing of the portion of the biomolecule.

13 Claims, 13 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 13

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KW
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17. Document ID: US 5538898 A

L1: Entry 17 of 17 File: USPT Jul 23, 1996

US-PAT-NO: 5538898

DOCUMENT-IDENTIFIER: US 5538898 A

TITLE: Method suitable for identifying a code sequence of a biomolecule

DATE-ISSUED: July 23, 1996

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Wickramasinghe; Hemantha K. Chappaqua NY Zenhausern; Frederic Mohegan Lake NY

US-CL-CURRENT: $\underline{436/94}$; $\underline{422/82.01}$, $\underline{422/82.05}$, $\underline{422/82.08}$, $\underline{422/82.12}$, $\underline{436/164}$, $\underline{436/177}$

ABSTRACT:

A method suitable for identifying a code sequence of a biomolecule. The method comprises the steps of using a near-field probe technique for generating a super-resolution chemical analysis of at least a portion of the biomolecule; and, correlating the chemical analysis with a broad spectral content of a referent biomolecule for generating code sequencing.

43 Claims, 13 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 13

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L1: Entry 12 of 17

File: USPT

Dec 28, 1999

DOCUMENT-IDENTIFIER: US 6007987 A

TITLE: Positional sequencing by hybridization

Brief Summary Paragraph Right (24):

Another embodiment of the invention is directed to replicated <u>arrays</u> and methods for replicating <u>arrays</u> of probes, preferably on a solid support, comprising the steps of synthesizing an <u>array of nucleic</u> acids each comprising a constant sequence of length C at a 3'-terminus and a random sequence of length R at a 5'-terminus, fixing the <u>array</u> to a first solid support, synthesizing a set of <u>nucleic</u> acids each comprising a sequence complimentary to the constant region of the <u>array</u>, hybridizing the <u>nucleic</u> acids of the set using the random sequences of the <u>array</u> as templates, <u>denaturing</u> the set of extended <u>nucleic</u> acids, and fixing the <u>denatured nucleic</u> acids of the set to a second solid <u>support</u> to create the replicated <u>array</u> of probes. The replicated array may be single-stranded or double-stranded, it may be fixed to a solid support or free in solution, and it is useful for sequencing, detecting or simply identifying target nucleic acids.

Brief Summary Paragraph Right (25):

The array is also useful for the purification of nucleic acid from a complex mixture for later identification and/or sequencing. A purification array comprises sufficient numbers of probes to hybridize and thereby effectively capture the target sequences from a complex sample. The hybridized array is washed to remove non-target nucleic acids and any other materials which may be present and the target sequences eluted by denaturing. From the elution, purified or semi-purified target sequences are obtained and collected. This collection of target sequences can then be subjected to normal sequencing methods or sequenced by the methods described herein.

Detailed Description Paragraph Right (30):

Due to the very large numbers of probes which comprise most useful arrays, there is a great deal of time spent in simply creating the array. It requires many hours of nucleic acid synthesis to create each member of the array and many hours of manipulations to place the array in an organized fashion onto any solid support such as those described previously. Once the master array is created, replicated arrays or slaves, can be quickly and easily created by the methods of the invention which take advantage of the speed and accuracy of nucleic acid polymerases. Basically, methods for replicating an array of single-stranded probes on a solid support comprise the steps of synthesizing an array of nucleic acids each comprising a constant sequence of length C at a 3'-terminus and a random sequence of length R at a 5'-terminus, fixing the array to a first solid support, synthesizing a set of nucleic acids each comprising a sequence complimentary to the constant sequence, hybridizing the nucleic acids of the set with the array, enzymatically extending the nucleic acids of the set using the random sequences of the array as templates, denaturing the set of extended nucleic acids, and fixing the denatured nucleic acids of the set to a second solid support to create the replicated array of single-stranded probes.